REMARKS

*Status of the Application*

Claims 1 and 4 have been amended, claim 5 has been cancelled, and claims 18-20 added, depending from claim 1. Claims 1, 4 and 18-20 are currently pending. Support for new claims 18-20 can be found, *inter alia*, in the Examples (pages 7-13). No new matter has been added.

*Claim rejections*

The Office has rejected claims 1, 4 and 5 as being anticipated by Riggs *et al.*, 2000 (Riggs "II" Riggs, P.J., M.K. Chelius, A.L. Iniguez, S.M. Kaeppler, and E.W. Triplett. 2000. Enhanced maize and wheat productivity by inoculation with diazotrophic endophytes. 8th International symposium on Nitrogen Fixation with non-Legumes; Sydney, Australia, December 3-5, 2000). Applicants respectfully traverse because Riggs *et al.* was not publicly available until *after* the priority date of the application.

Riggs *et al.* is an abstract of an address that was presented by an inventor at a conference on December 3-7, 2000 in Sydney Australia. The abstract was not available until December 5, 2000, while the priority date for the application is December 4, 2000. Applicant proffers the attached Affidavit from Dr. Eric W. Triplett, dated August 29, 2006, in which Dr. Triplett avers to the date of public availability of Riggs *et al.* (II) (*see* Appendix A). Therefore, Riggs *et al.* (II) is not an applicable reference, and the rejection is respectfully requested to be withdrawn.

The Office has rejected claims 1, 4 and 5 as being anticipated by Remus *et al.*, 2000 (Remus, R., Ruppel, S., Jacob, H.-J., Hecht-Buchholz, C. and Merbach, W. 2000. Colonization behaviour of two enterobacterial strains on cereals. *Biol. Fertil. Soils* 30:550-557). Applicants respectfully traverse. Remus *et al.* do not teach each and every limitation of the claims to be anticipatory because the *K. pneumoniae* inoculation had no effect, or even an inhibitory effect, on plant growth in wheat. For this same reason, Remus *et al.* teach away from the claimed invention of *K. pneumoniae* inoculants that enhance plant growth, rendering the claims non-obvious.

Firstly, Applicants note that claims 1 and 4 have been amended to delete "mutants," about which the Office complained in this rejection. Claim 5 has been cancelled, thus obviating the rejection with regard to that claim.

Secondly, Applicants point out the claimed *K. pneumoniae* strains (342 and zmvsy) were isolated from very different regions than the CC12/12 strain of Remus *et al.* The 342 strain was isolated from a very nitrogen efficient line of maize from Mexico cultured in a greenhouse in Madison, Wisconsin, while the zmvsy strain was isolated from a single maize plant grown on a farm in Madison, Wisconsin.

The origin of the CC12/12 line is a story full of twists and illustrates the challenges in non-medical bacterial taxonomy—and also supports Applicants' argument that the strain neither anticipates nor renders obvious the claimed strains.

According to Dr. Ruppel (personal communication), the CC12/12 strain was isolated from the rhizospheres of the grass *Ammophila arenaria*, which were growing in the sand dunes near the coast of the Baltic sea in Germany. Upon depositing with bacterial bank Zentralinstitut für Mikrobiologie und Experimentelle Therapie (ZIMET 11252. ZIMET was later incorporated into the Deutsche Sammlung von Mikroorganismen und Zellkulturen GmbH (DSMZ)), the first try to classify the strain CC12/12 suggested perhaps *Serratia rubidea* (not *K. pneumoniae*) with a similarity of about 78% which, according to Dr. Ruppel, "is nearly nothing." After some time, two more strain collections tried again to classify this strain. They named it *Klebsiella pneumoniae*, but based on only about 82% similarity to the type strains. For a more secure taxonomy, a similarity of at least 97% is ideal. The CC12/12 strain was first published as *Serratia rubidea* in Ruppel, S. 1991: S*erratia rubidea* - an associative plant growth promoting nitrogen fixing microorganism. *Zentralbl. Mikrobiol.* 146: 297-303, which article is supplied in a supplemental information disclosure statement filed with this response.

Remus *et al.* report on their experiments using *Pantoea agglomerans* D5/23 and *Klebsiella pneumoniae* CC12/12, and their effects after their inoculation in wheat cultivars (*see* Abstract). They found that while *K. pneumoniae* effectively colonized the roots, and more so than *P. agglomerans*, only *P. agglomerans* markedly increased root growth (*see* Abstract; also *see* page 552, column 2, second paragraph and Table 2). Furthermore, *K. pneumoniae* failed to colonize any shoots (page 552, column 2, paragraph 3, 3rd sentence). Most telling, in Table 2 which reports in part the effects of *K. pneumoniae* inoculation on root and shoot growth of spring wheat cv. Eta, *K. pneumoniae* inoculation did *not* increase shoot mass at all (control: 1.97 g/plant *vs.* experimental: 1.84 g/plant; difference = -0.13, a decrease of approximately 15%).

The Office argues that Remus *et al.* disclose a *K. pneumoniae* strain that is suitable as an inoculum for plant and "which appears to be identical to the presently claimed strain," and then points to page 553. Without further clarification, Applicants believe the Office is pointing to Table 2, discussed immediately above.

The claimed strains are *not* identical, or even obvious variants, because the claimed strains enhance plant growth. In experiments that measured the effect of the claimed *K. pneumoniae* strains to enhance shoot weight in wheat (experiments that look at the most analogous variables as Remus *et al.* examined), the inventors inoculated three cultivars of wheat, Trenton, Rus and Stoa (Example 1, pages 7-8 of the Application as filed). In the case of the Trenton cultivar, *K. pneumoniae* inoculation increased dry shoot weight dramatically: with *K. pneumoniae* 342, the average weight per plant increased almost 200% (from 0.257 mg to 0.789 mg), and with *K. pneumoniae* zmvsy, almost a 95% increase (from 0.257 mg to 0.500 mg) (*see* Table 1). In the other cases, increases in dry shoot weight were observed in the Russ cultivar, and for Stoa (with *K.*

*pneumoniae* 342). In the case of *K. pneumoniae* zmvsy and the Stoa cultivar, the difference is slight (-6%) as to be considered insignificant.

The Office has not presented a reasoned, rational statement as to how the strain disclosed by Remus *et al.* is even remotely *identical*, and thus anticipatory, to the strains claimed when the Remus *et al.* strain has at best *no effect* on shoot growth in wheat, and more likely, a *negative* effect. Furthermore, the fact that the taxonomy of the CC12/12 strain, coupled with its distinctly different geographic region from where it was isolated, makes it even less likely that the CC12/12 strain is anticipatory of the zmvsy strain. Clearly, the strains are *not* identical, and Remus *et al.* cannot anticipate the present claims.

Furthermore, because Remus *et al.* demonstrated (1) equivocal/negative effects regarding shoot growth and *K. pneumoniae* inoculation and (2) an increase in root growth that was modest when compared to that seen with *P. agglomerans* inoculation (an increase of 0.17 g *vs.* 0.48 g, respectively; *see* Table 2, page 543), Remus *et al.* effectively teach away from *K. pneumoniae* inoculations for enhancing plant growth. One of skill in the art would have, based on Remus *et al.*'s disclosure, pursued *P. agglomerans* inoculations. The claims are therefore not obvious in view of Remus *et al.*; Applicants pray the Office to withdraw the rejection.

The Office has rejected claims 1, 4 and 5 as anticipated under 35 USC 102(b), or alternatively, as obvious under 35 USC 103(a) by Haahtela *et al.* 1988 (Haahtela, K, Laakso, T., Nurmiaho-Lassila, E.-L. and Korhonen, T.K. 1988. Effects of inoculation of *Poa pratensis* and *Triticum aestivum* with root-associated, $N_2$-fixing Klebsiella, Enterobacter and Azospirillum." *Plant Soil* 106:239-248). Applicants respectfully traverse. Haahtela *et al.* fail to disclose the claimed *K. pneumoniae* strains because they are not identical: they do not have the same plant growth-enhancing activities, and are therefore also non-obvious.

Applicants first note that the *K. pneumoniae* strain that Haahtela *et al.* studied, *K. pneumoniae* Pp., was isolated from blue grass (*Poa pratensis*) in Finland in the early 1980s (Haahtela, K., Kirsti, K. and Sundman, V. 1983. Nitrogenase activity (acetylene reduction) of root-associated, cold-climate *Azospirillum, Enterobacter, Klebsiella,* and *Pseudomonas* species during growth on various carbon sources and at various partial pressures of oxygen. *App. Environ. Microbiol.* 45:563-570, p. 564, column 2; and Haahtela, K. and Korhonen, T.K. 1985. *In vitro* adhesion of $N_2$-fixing enteric bacteria to roots of grasses and cereals. *App. Environ. Microbiol.* 49:1186-1190, page 1186, column 2, 1st paragraph), while the claimed strains were isolated as described above.

Haahtela *et al.* is directed to studies of inoculations of *K. pneumoniae*, *Klebsiella terrigena, Enterobacter agglomerans* and *Azospirillum lipoferum* in blue grass (*Poa pratensis*) and wheat. The investigators found, as reported in Tables 2 and 3 on page 245 that while *K. pneumoniae* increased root hair growth moderately (*see* Table 1, page 242), such inoculations did not increase dry matter yield significantly when compared to controls, neither in blue grass (1.175 ± 0.247 g (experimental) *vs.* 1.349 ± 0.401 g (control)) nor in wheat (2.721 ± 0.189 g (experimental) *vs.* 2.668 ± 0.308 g (control)). They did not find a direct correlation between increased nitrogen assimilation by the plants and increases in growth; for example, *K. pneumoniae* inoculations

of *P. pratensis* did not increase in dry matter yield (in fact, Table 2, page 245 reports a decrease), but had the most striking and statistically significant increase in nitrogen content (Table 2, page 245). These results suggest that even though a bacterium may have the ability to fix nitrogen, and because of its association with a plant, the plant may have an enhanced nitrogen content, the bacterium may have no effect whatsoever on dry shoot weight or seed/grain production.

While the inventors did not look at root hair growth and dry matter yield in blue grass, and looked at only dry shoot weight, but not root hair growth, in wheat, the Haahtela *et al.*'s *K. pneumoniae* strain is clearly different. Firstly, Haahtela *et al.*'s *K. pneumoniae* strain only slightly increased dry matter yield in wheat (Table 3, page 245, experimental: $2.721 \pm 0.189$; control: $2.668 \pm 0.309$; a 0.053 increase that was reported to be insignificant). Secondly, the inventors inoculated three cultivars of wheat, Trenton, Rus and Stoa and examined dry shoot weight, the most analogous variable examined by Haahtela *et al.* (Example 1, pages 7-8 of the Application as filed). In the case of the Trenton cultivar, *K. pneumoniae* inoculation increased dry shoot weight dramatically: with *K. pneumoniae* 342, the average weight per plant increased almost 200% (from 0.257 mg to 0.789 mg), and with *K. pneumoniae* zmvsy, almost a 95% increase (from 0.257 mg to 0.500 mg) (*see* Table 1). In the other cases, increases in dry shoot weight were observed in the Russ cultivar, and for Stoa (with *K. pneumoniae* 342). In the case of *K. pneumoniae* zmvsy and the Stoa cultivar, the difference is slight (-6%) as to be considered insignificant. Haahtela *et al.* failed to achieve any such results in wheat.

The Office has not presented a reasoned, rational statement as to how the strain disclosed by Haahtela *et al.* is even remotely *identical* to the strains claimed when the Haahtela *et al.* strain has at best only a slight effect on shoot growth in wheat, and more likely, *no* effect. Clearly, the strains are *not* identical, and Haahtela *et al.* cannot anticipate the present claims.

Furthermore, because Haahtela *et al.* demonstrated slight/equivocal effects regarding shoot growth and *K. pneumoniae* inoculation, Haahtela *et al.* effectively teach away from *K. pneumoniae* inoculations for enhancing plant growth. One of skill in the art would have, based on Haahtela *et al.*'s disclosure, pursued other nitrogen-fixing bacteria to increase shoot growth. The claims are therefore not obvious in view of Remus *et al.*; Applicants pray the Office to withdraw the rejection.

Regarding the Office's repeated argument that "the prior art strains, which is of the same species *K. pneumoniae* as that claimed, likewise shares the property of at least being able to colonize grains and promote plant growth" (*see* Action of May 14, 2007, pages 4 and 5), Applicants traverse. The argument fails on two counts, among others. First, Applicants note that being the same *species* is not the same as being the same *strain*. This basic notion that strains differ is borne out even in the taxonomic nomenclature, which includes the strain designation in the names. The prior art examined *K. pneumoniae* Pp and CC12/12 strains, while the inventors are claiming zmvsy and 342 strains; thus the names alone indicate to one of skill in the art that they are inherently and significantly different. Secondly, the cited prior art and the inventors' own results

demonstrate clear differences; most notably, the cited prior art strains of *K. pneumoniae*, at best, have no effect on enhancing plant growth, and in one case, appears to inhibit it; thus the strains are clearly not the same.

Regarding the Office's repeated argument that the "recitation of distinct ATCC numbers does not distinguish an invention, since any individual may buy a strain at the ATCC and redeposit it under a fresh number" (*see* Action of May 14, 2007, pages 3 and 5), Applicants traverse.

The Office seems to be insinuating that Applicants are not meeting their duty of candor. If the Examiner has personal knowledge of such activities, she should present the information clearly (including the relevant ATCC deposit numbers) so that Applicants can investigate the activity. Applicants have no interest in obtaining patents that are unenforceable.

Furthermore, the argument is untenable.

Firstly, the ATCC would appear to have no interest in collecting duplicate strains as such an activity would strain scant resources: "ATCC welcomes deposits of valuable research materials and our goal is to have a broad and comprehensive collection. Unfortunately, owing to limited resources, we cannot accept for accession all materials that may be offered" (http://www.atcc.org/common/deposits/MakeDeposit.cfm, last visited August 7, 2007). The ATCC elaborates that the "bacteriology collection specifically seeks newly identified type strains . . . [and] environmental isolates that have truly unique properties . . ." (https://www.atcc.org/common/technicalInfo/faqBacteriology.cfm; last visited August 7, 2007).

Secondly, Applicants have complied with the duty of candor as prescribed by 37 CFR 1.56. Applicants have filed appropriate Information Disclosure Statements (March 24, 2005 and February 8, 2006). These filings are in concert with the Office's goal as explained in *MPEP* 2001.04, "The Office strives to issue valid patents. *The Office has both an obligation not to unjustly issue patents and an obligation not to unjustly deny patents.*" [emphasis added]. If Applicants knew of similar strain deposits at the ATCC, they would have disclosed them to the Office. In fact, Applicants have exhibited their willingness to be explicitly candid with the Office, witness the specification, "Bacterial strains *H. seropedicae* Z152 (ATCC No. 35894) and *G. diazotrophicus* PA15 (ATCC No. 49037) were both previously known and available from the ATCC . . . " (page 4, paragraph 18).

Thirdly, the Office has provided no reasonable, rational argument why any Applicant would perpetuate such a fraud that exhausts ATCC resources and endangers the enforceability and validity of any patents issued thereon.

Applicants request the argument to be withdrawn.

## REQUEST FOR RECONSIDERATION

Having addressed all outstanding rejections and overcome them, reconsideration and withdrawal of all claim rejections are respectfully requested. Applicants believe that the present application is in condition for allowance. Should the Examiner have any questions or would like to discuss any matters in connection with the present application, the Examiner is invited to contact the undersigned at

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APPENDIX A

08/29/06 TUE 12:36 FAX 3528480956 MICRO&CELL SCI 002

Affidavit

I, Eric W. Triplett, being a U.S. citizen residing at 9244 SW 31st Place, Gainesville, FL 32608 and knowing about the criminal nature of a false affidavit declare in lieu of an oath:

1. I am one of the inventors of European Patent Application No. 01 996 114.3-2103 entitled "Bacterial inoculants for enhancing plant growth," which has been assigned to Wisconsin Alumni Research Foundation.

2. I am one of the authors of P.J. Riggs et al., "Enhanced maize productivity by inoculation with diazotrophic bacteria," *Australian Journal of Plant Physiology* 28(9):829 – 836, the abstract of which is referred to as D1 in the European Search Report under Rule 112 EPC.

3. The contents of D1 were presented by me at the 8th International Symposium on Nitrogen Fixation with Non-Legumes in Sydney, Australia on December 5, 2000.

4. All statements made herein of my own knowledge are true and that all statements made on information and belief are true.

Eric W. Triplett

Eric W. Triplett

8/29/06

Date